

What is Claimed:

1. A pharmaceutical carrier or excipient system useful for preparing a pharmaceutical formulation, the carrier or excipient system comprising:

a) a filler and disintegrant component comprising from about 5% to about 82% by weight of the pharmaceutical formulation, of which from about 4% to about 40% by weight of the total formulation comprises one or more pharmaceutically acceptable disintegrants;

b) optionally, a wetting agent comprising from about 0.2 to about 5% of the pharmaceutical formulation;

c) a lubricant comprising from about 0.2% to about 10% of the pharmaceutical formulation; and

d) optionally, a glidant comprising from about 0.1% to about 10% of the pharmaceutical formulation.

2. The pharmaceutical carrier or excipient system of Claim 1 further comprising from about 0.5% to about 15% by weight of an antioxidant.

3. The pharmaceutical carrier or excipient system of Claim 2 wherein the antioxidant is selected from ascorbic acid, sodium ascorbate, ascorbyl palmitate, or mixtures thereof.

4. A pharmaceutical composition comprising a pharmaceutically effective amount of an active pharmacological agent and carrier or excipient system, the carrier or excipient system comprising:

a) a filler and disintegrant component comprising from about 5% to about 82% by weight of the pharmaceutical formulation, of which from about 4% to about 40% by weight of the total formulation comprises one or more pharmaceutically acceptable disintegrants;

b) optionally, a wetting agent comprising from about 0.2 to about 5% of the pharmaceutical formulation;

R₁ is selected from H, OH or the C₁-C₁₂ esters or C₁-C₁₂ alkyl ethers thereof, benzyloxy, or halogen; or C₁-C₄ halogenated ethers;

R₂, R₃, R₅ and R₆ are independently selected from H, OH or the C₁-C₁₂ esters or C₁-C₁₂ alkyl ethers thereof, halogens, or C₁-C₄ halogenated ethers, cyano, C₁-C₆ alkyl, or trifluoromethyl, with the proviso that, when R₁ is H, R₂ is not OH;

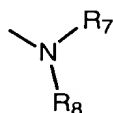
R₄ is selected from H, OH or the C₁-C₁₂ esters or C₁-C₁₂ alkyl ethers thereof, halogens, or C₁-C₄ halogenated ethers, benzyloxy, cyano, C₁-C₆ alkyl, or trifluoromethyl;

X is selected from H, C₁-C₆ alkyl, cyano, nitro, trifluoromethyl, halogen;

n is 1, 2 or 3;

Y is selected from:

a) the moiety:



wherein R₇ and R₈ are independently selected from the group of H, C₁-C₆ alkyl, or phenyl optionally substituted by CN, C₁-C₆ alkyl, C₁-C₆ alkoxy, halogen, -OH, -CF₃, or -OCF₃;

b) a five-membered saturated, unsaturated or partially unsaturated heterocycle containing up to two heteroatoms selected from the group consisting of -O-, -NH-, -N(C₁C₄ alkyl)-, -N=, and -S(O)_m-, wherein m is an integer of from 0-2, optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ acyloxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H-, -CN-, -CONHR₁-, -NH₂-, C₁-C₄ alkylamino, di(C₁-C₄)alkylamino, -NHSO₂R₁-, -NHCOR₁-, -NO₂, and phenyl optionally substituted with from one to three (C₁-C₄)alkyl groups;

c) a six-membered saturated, unsaturated or partially unsaturated heterocycle containing up to two heteroatoms selected from the group consisting of -O-, -NH-, -N(C₁C₄ alkyl)-, -N=, and -S(O)_m-, wherein m is an integer of from 0-2, optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ acyloxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H-, -CN-, -CONHR₁-, -NH₂-

, C₁-C₄ alkylamino, di(C₁-C₄)alkylamino, -NHSO₂R₁-, -NHCOR₁-, -NO₂, and phenyl optionally substituted with from one to three (C₁-C₄)alkyl groups;

d) a seven-membered saturated, unsaturated or partially unsaturated heterocycle containing up to two heteroatoms selected from the group consisting of -O-, -NH-, -N(C₁C₄ alkyl)-, -N=, and -S(O)_m-, wherein m is an integer of from 0-2, optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ acyloxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H-, -CN-, -CONHR₁-, -NH₂-, C₁-C₄ alkylamino, di(C₁-C₄)alkylamino, -NHSO₂R₁-, -NHCOR₁-, -NO₂, and phenyl optionally substituted with from one to three (C₁-C₄)alkyl groups; or

e) a bicyclic heterocycle containing from 6-12 carbon atoms either bridged or fused and containing up to two heteroatoms selected from the group consisting of -O-, -NH-, -N(C₁C₄ alkyl)-, and -S(O)_m-, wherein m is an integer of from 0-2, optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ acyloxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H-, -CN-, -CONHR₁-, -NH₂-, C₁-C₄ alkylamino, di(C₁-C₄)alkylamino, -NHSO₂R₁-, -NHCOR₁-, -NO₂, and phenyl optionally substituted with from one to three (C₁-C₄)alkyl groups; or a pharmaceutically acceptable salt thereof.

8. The pharmaceutical composition of Claim 7 wherein in the compound of the formulae I or II:

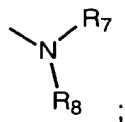
R₁ is selected from H, OH or the C₁-C₁₂ esters or alkyl ethers thereof, benzyloxy, or halogen;

R₂, R₃, R₅, and R₆ are independently selected from H, OH or the C₁-C₁₂ esters or alkyl ethers thereof, halogen, cyano, C₁-C₆ alkyl, or trihalomethyl; with the proviso that, when R₁ is H, R₂ is not OH;

R₄ is selected from H, OH or the C₁-C₁₂ esters or alkyl ethers thereof, benzyloxy, halogen, cyano, C₁-C₆ alkyl, or trihalomethyl;

X is selected from H, C₁-C₆ alkyl, cyano, nitro, trifluoromethyl, halogen;

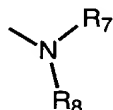
Y is the moiety



R₇ and R₈ are selected independently from H, C₁-C₆ alkyl, or combined by -(CH₂)_p, wherein p is an integer of from 2 to 6, so as to form a ring, the ring being optionally substituted by up to three substituents selected from the group of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H, -CN, -CONH(C₁-C₄), -NH₃, C₁-C₄ alkylamino, C₁-C₄ dialkylamino, -NHSO₂(C₁-C₄), -NHCO(C₁-C₄), and -NO₃; or a pharmaceutically acceptable salt thereof.

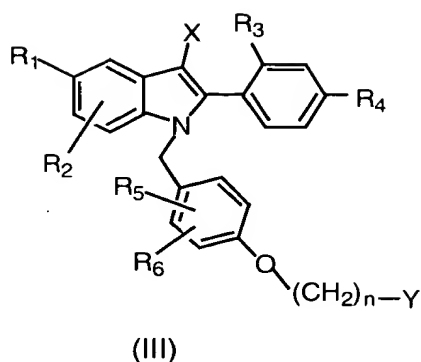
9. The pharmaceutical formulation of Claim 8 wherein, in the compound of the formulae I or II, the ring formed by a the combination of R₇ and R₈ by -(CH₂)_p- is selected from aziridine, azetidine, pyrrolidine, piperidine, hexamethyleneamine or heptamethyleneamine.

10. The method of Claim 7 utilizing a compound of the formulae I or II, wherein R₁ is OH; R₂ - R₆ are as defined in Claim 1; X is selected from the group of Cl, NO₂, CN, CF₃, or CH₃; and Y is the moiety

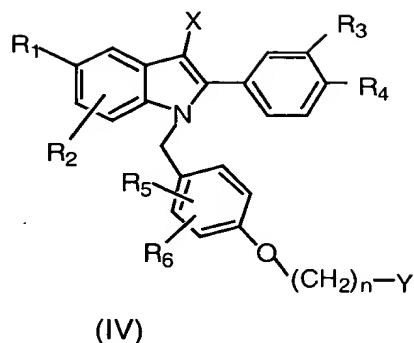


and R₇ and R₈ are concatenated together as -(CH₂)_r-, wherein r is an integer of from 4 to 6, to form a ring optionally substituted by up to three substituents selected from the group of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H, -CN, -CONH(C₁-C₄)alkyl, -NH₂, C₁-C₄ alkylamino, di(C₁-C₄)alkylamino, -NHSO₂(C₁-C₄)alkyl, -NHCO(C₁-C₄)alkyl, and -NO₂; or a pharmaceutically acceptable salt thereof.

11. A pharmaceutical composition of Claim 4 wherein the active pharmacological agent is a compound of the formulae (III) or (IV):



or



wherein the substituents R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , n , X , and Y are as defined in Claim 7, or a pharmaceutically acceptable salt thereof.

12. A pharmaceutical composition of Claim 11 wherein:

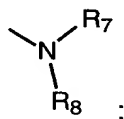
R_1 is selected from H, OH or the C₁-C₁₂ esters or alkyl ethers thereof, benzyloxy, or halogen;

R_2 , R_3 , R_5 , and R_6 are independently selected from H, OH or the C₁-C₁₂ esters or alkyl ethers thereof, halogen, cyano, C₁-C₆ alkyl, or trihalomethyl, preferably trifluoromethyl, with the proviso that, when R_1 is H, R_2 is not OH;

R_4 is selected from H, OH or the C₁-C₁₂ esters or alkyl ethers thereof, benzyloxy, halogen, cyano, C₁-C₆ alkyl, or trihalomethyl;

X is selected from H, C₁-C₆ alkyl, cyano, nitro, trifluoromethyl, halogen;

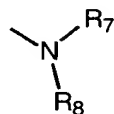
Y is the moiety



R_7 and R_8 are selected independently from H, C₁-C₆ alkyl, or combined by $-(CH_2)_p-$, wherein p is an integer of from 2 to 6, so as to form a ring, the ring being optionally substituted by up to three substituents selected from the group of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, $-CO_2H$, $-CN$, $-CONH(C_1-C_4)$, $-NH_3$, C₁-C₄ alkylamino, C₁-C₄ dialkylamino, $-NHSO_2(C_1-C_4)$, $-NHCO(C_1-C_4)$, and $-NO_3$;

or a pharmaceutically acceptable salt thereof.

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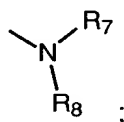
R₁ is selected from H, OH or the C₁-C₁₂ esters or alkyl ethers thereof, benzyloxy, or halogen;

R₂, R₃, R₅, and R₆ are independently selected from H, OH or the C₁-C₁₂ esters or alkyl ethers thereof, halogen, cyano, C₁-C₆ alkyl, or trihalomethyl, preferably trifluoromethyl, with the proviso that, when R₁ is H, R₂ is not OH;

R₄ is selected from H, OH or the C₁-C₁₂ esters or alkyl ethers thereof, benzyloxy, halogen, cyano, C₁-C₆ alkyl, or trihalomethyl;

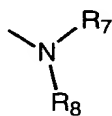
X is selected from H, C₁-C₆ alkyl, cyano, nitro, trifluoromethyl, halogen;

Y is the moiety



R₇ and R₈ are selected independently from H, C₁-C₆ alkyl, or combined by -(CH₂)_p-, wherein p is an integer of from 2 to 6, so as to form a ring, the ring being optionally substituted by up to three substituents selected from the group of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H, -CN, -CONH(C₁-C₄), -NH₃, C₁-C₄ alkylamino, C₁-C₄ dialkylamino, -NHSO₂(C₁-C₄), -NHCO(C₁-C₄), and -NO₃; or a pharmaceutically acceptable salt thereof.

17. A pharmaceutical composition of Claim 15 wherein R₁ is OH; R₂ - R₆ are as defined above; X is selected from the group of Cl, NO₂, CN, CF₃, or CH₃; and Y is the moiety

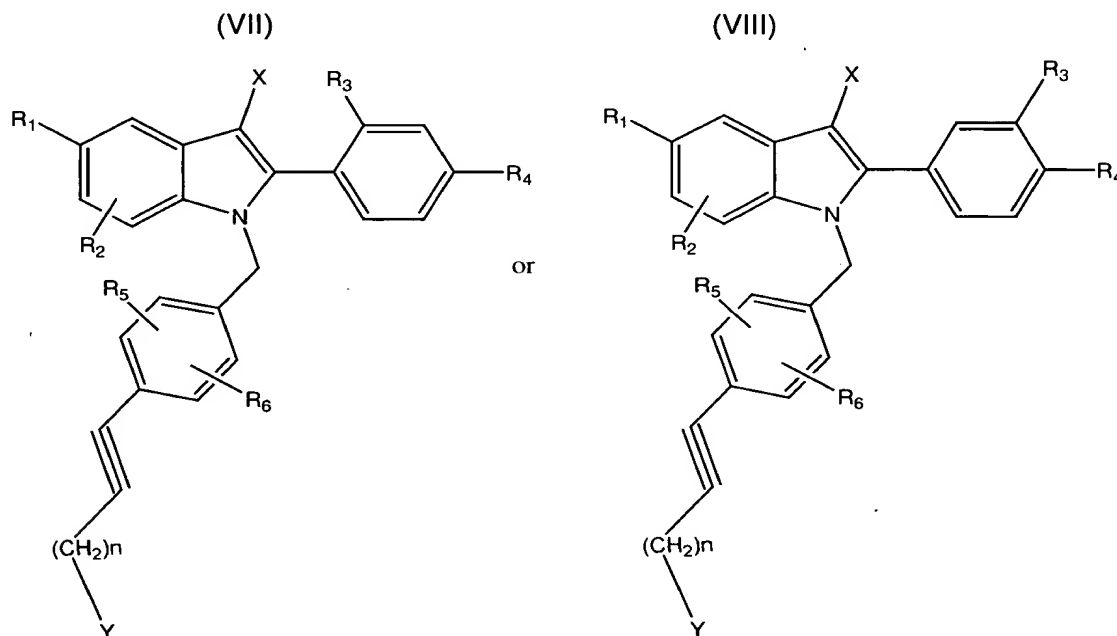


and R₇ and R₈ are concatenated together as -(CH₂)_r-, wherein r is an integer of from 4 to 6, to form a ring optionally substituted by up to three substituents selected from the group of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H, -CN, -CONH(C₁-C₄)alkyl, -NH₂, C₁-C₄ alkylamino, di(C₁-C₄)alkylamino, -NHSO₂(C₁-C₄)alkyl, -NHCO(C₁-C₄)alkyl, and -NO₂; or a pharmaceutically acceptable salt thereof.

18. A pharmaceutical composition of Claim 15 wherein R₇ and R₈ are concatenated together as -(CH₂)_p-, wherein p is an integer of from 2 to 6, preferably 4 to 6, the ring so formed is optionally substituted with 1-3 substituents selected from a group containing C₁-C₃ alkyl, trifluoromethyl, halogen, hydrogen, phenyl, nitro, -CN.

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19. A pharmaceutical composition of Claim 4 wherein the active pharmacological agent is a compound of the formulae (VII) or (VIII):



wherein the variable substituents including R₁, R₂, R₃, R₄, R₅, R₆, n, X, and Y are as defined in Claim 7, or a pharmaceutically acceptable salt thereof.

20. A pharmaceutical composition of Claim 19 wherein:

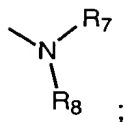
R₁ is selected from H, OH or the C₁-C₁₂ esters or alkyl ethers thereof, benzyloxy, or halogen;

R₂, R₃, R₅, and R₆ are independently selected from H, OH or the C₁-C₁₂ esters or alkyl ethers thereof, halogen, cyano, C₁-C₆ alkyl, or trihalomethyl, preferably trifluoromethyl, with the proviso that, when R₁ is H, R₂ is not OH;

R₄ is selected from H, OH or the C₁-C₁₂ esters or alkyl ethers thereof, benzyloxy, halogen, cyano, C₁-C₆ alkyl, or trihalomethyl;

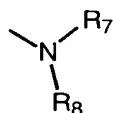
X is selected from H, C₁-C₆ alkyl, cyano, nitro, trifluoromethyl, halogen;

Y is the moiety



R₇ and R₈ are selected independently from H, C₁-C₆ alkyl, or combined by -(CH₂)_p-, wherein p is an integer of from 2 to 6, so as to form a ring, the ring being optionally substituted by up to three substituents selected from the group of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H, -CN, -CONH(C₁-C₄), -NH₃, C₁-C₄ alkylamino, C₁-C₄ dialkylamino, -NHSO₂(C₁-C₄), -NHCO(C₁-C₄), and -NO₃; or a pharmaceutically acceptable salt thereof.

21. A pharmaceutical composition of Claim 19 wherein R₁ is OH; R₂ - R₆ are as defined above; X is selected from the group of Cl, NO₂, CN, CF₃, or CH₃; and Y is the moiety



and R₇ and R₈ are concatenated together as -(CH₂)_r-, wherein r is an integer of from 4 to 6, to form a ring optionally substituted by up to three substituents selected from the group of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H, -CN, -CONH(C₁-C₄)alkyl, -NH₂, C₁-C₄ alkylamino, di(C₁-C₄)alkylamino, -NHSO₂(C₁-C₄)alkyl, -NHCO(C₁-C₄)alkyl, and -NO₂; or a pharmaceutically acceptable salt thereof.

22. A pharmaceutical composition of Claim 19 wherein R₇ and R₈ are concatenated together as -(CH₂)_p-, wherein p is an integer of from 2 to 6, preferably 4 to 6, the ring so formed is optionally substituted with 1-3 substituents selected from a group containing C₁-C₃ alkyl, trifluoromethyl, halogen, hydrogen, phenyl, nitro, -CN.

23. A pharmaceutical composition of Claim 4 wherein the active pharmacological agent is 1-[4-(2-Azepan-1yl-ethoxy)-benzyl]-2-(4-hydroxy-phenyl)-3-methyl-1H-indol-5-ol or a pharmaceutically acceptable salt thereof.

24. A pharmaceutical composition of Claim 4 wherein the active pharmacological agent is 2-(4-Hydroxy-phenyl)-3-methyl-1-(4-(2-piperidin-1-yl-ethoxy)-benzyl]-1H-indol-5-ol or a pharmaceutically acceptable salt thereof.

25. A pharmaceutical composition of Claim 4 wherein the active pharmacological agent is selected from the group of raloxifene, tamoxifen, droloxifene, arzoxifene or CP 336156, or a pharmaceutically acceptable salt thereof.

26. A pharmaceutical composition comprising:

a) a pharmaceutically effective amount of 1-[4-(2-Azepan-1yl-ethoxy)-benzyl]-2-(4-hydroxy-phenyl)-3-methyl-1H-indol-5-ol or 2-(4-Hydroxy-phenyl)-3-methyl-1-(4-(2-piperidin-1-yl-ethoxy)-benzyl]-1H-indol-5-ol, or a pharmaceutically acceptable salt thereof;

b) a filler and disintegrant component comprising between about 50% and about 80% of the formulation, with from about 4% to about 40% of the formulation comprising one or more disintegrant agents;

c) a wetting agent comprising between about 0.5% and about 2.5% of the formulation;

d) a lubricant comprising between about 0.2% and about 5% of the formulation; and

e) a glidant comprising between about 0.1% and about 5% of the formulation.

27. The pharmaceutical composition of Claim 26 further comprising an antioxidant at a concentration of from about 0.5% to about 5% by weight of the composition, the antioxidant being selected from the group of ascorbic acid, sodium ascorbate, ascorbyl palmitate, or mixtures thereof.

28. The pharmaceutical composition of Claim 26 further being coated with a film coating comprising from about 0.3% to about 8% by weight of the composition.

29. A pharmaceutical composition comprising:

a) a pharmaceutically effective amount of 1-[4-(2-Azepan-1yl-ethoxy)-benzyl]-2-(4-hydroxy-phenyl)-3-methyl-1H-indol-5-ol or 2-(4-Hydroxy-phenyl)-3-methyl-1-(4-(2-piperidin-1-yl-ethoxy)-benzyl]-1H-indol-5-ol, or a pharmaceutically acceptable salt thereof;

b) a filler and disintegrant component of one or more pharmaceutically acceptable fillers and disintegrants comprising between about 54% and about 87% of the formulation, the disintegrants therein comprising from about 25% to about 35% of the formulation, by weight;

5 c) a wetting agent comprising between about 0.55% and about 2.7% of the formulation;

d) a lubricant comprising between about 0.2% and about 5.5% of the formulation;
and

10 e) a glidant comprising between about 0.1% and about 5.5% of the formulation.

30. The pharmaceutical composition of Claim 29 further comprising an antioxidant at a concentration of from about 0.5% to about 5% by weight of the composition, the antioxidant being selected from the group of ascorbic acid, sodium ascorbate, ascorbyl palmitate, or a mixture thereof.

31. The pharmaceutical composition of Claim 29 further being coated with a film coating comprising from about 0.3% to about 8% by weight of the composition.

32. A pharmaceutical composition comprising, by weight:
- a) from about 2% to about 8% 1-[4-(2-Azepan-1yl-ethoxy)-benzyl]-2-(4-hydroxy-phenyl)-3-methyl-1H-indol-5-ol or 2-(4-Hydroxy-phenyl)-3-methyl-1-(4-(2-piperidin-1-yl-ethoxy)-benzyl]-1H-indol-5-ol, or a pharmaceutically acceptable salt thereof;
 - b) lactose from about 32% to about 38%;
 - c) microcrystalline cellulose from about 32% to about 38%;
 - d) pregelatinized starch from about 12% to about 16%;
 - e) ascorbic acid from about 1% to about 2%;
 - f) sodium lauryl sulfate from about 1% to about 2%;
 - g) sodium starch glycolate from about 4% to about 8%;
 - h) silicon dioxide from about 0.1% to about 0.2%; and
 - i) magnesium stearate from about 0.3% to about 0.7%.

33. A pharmaceutical composition comprising, by weight:
- a) from about 0.1% to about 25% 1-[4-(2-Azepan-1yl-ethoxy)-benzyl]-2-(4-hydroxy-phenyl)-3-methyl-1H-indol-5-ol or 2-(4-Hydroxy-phenyl)-3-methyl-1-(4-(2-piperidin-1-yl-ethoxy)-benzyl]-1H-indol-5-ol, or a pharmaceutically acceptable salt thereof;
 - b) from about 20% to about 80% lactose;
 - c) from about 4% to about 40% pregelatinized starch;
 - d) from about 0.2% to about 5% sodium lauryl sulfate;
 - e) from about 0.5% to about 15% ascorbic acid;
 - f) from about 0.1% to about 10% silicon dioxide; and
 - g) from about 0.2% to about 10% magnesium stearate.

34. A pharmaceutical composition of Claim 33 comprising, by weight:
- a) from about 5% to about 18% 1-[4-(2-Azepan-1yl-ethoxy)-benzyl]-2-(4-hydroxy-phenyl)-3-methyl-1H-indol-5-ol or 2-(4-Hydroxy-phenyl)-3-methyl-1-(4-(2-piperidin-1-yl-ethoxy)-benzyl]-1H-indol-5-ol, or a pharmaceutically acceptable salt thereof;
 - b) from about 47% to about 77% lactose;
 - c) from about 25% to about 35% pregelatinized starch;
 - d) from about 1% to about 2% sodium lauryl sulfate;
 - e) from about 1% to about 3% ascorbic acid;
 - f) from about 0.1% to about 0.5% silicon dioxide; and
 - g) from about 0.2% to about 0.5% magnesium stearate.